

## ORIGINAL ARTICLE

# The impact of surgical site infection on hospitalisation, treatment costs, and health-related quality of life after vascular surgery

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## Abstract

Surgical site infections (SSI) substantially increase costs for healthcare providers because of additional treatments and extended patient recovery. The objective of this study was to assess the cost and health-related quality of life impact of SSI, from the perspective of a large teaching hospital in England. Data were available for 144 participants undergoing clean or clean-contaminated vascular surgery. SSI development, length of hospital stay, readmission, and antibiotic use were recorded over a 30-day period. Patient-reported EQ-5D scores were obtained at baseline, day 7 and day 30. Linear regressions were used to control for confounding variables. A mean SSI-associated length of stay of 9.72 days resulted in an additional cost of £3776 per patient (including a mean antibiotic cost of £532). Adjusting for age, smoking status, and procedure type, SSI was associated with a 92% increase in length of stay ( $P < 0.001$ ). The adjusted episode cost was £3040. SSI reduced patient utility between baseline and day 30 by 0.156 ( $P = 0.236$ ). Readmission rates were higher with SSI ( $P = 0.017$ ), and the rate to return to work within 90 days was lower. Therefore, strategies to reduce the risk of surgical site infection for high-risk vascular patients should be investigated.

## KEYWORDS

cost, health-related quality of life, infection, regression, vascular surgery

## 1 | INTRODUCTION

In the UK, surgical site infection (SSI) accounts for up to 1 in 7 hospital acquired infections.<sup>1</sup> Within vascular surgery, SSI may complicate up to 40% of procedures, with those undergoing lower limb revascularisation and major

limb amputations at the highest risk.<sup>2-4</sup> This elevated incidence is thought to relate to the high rates of comorbidities in vascular patients, such as diabetes, obesity, increasing age, malnutrition, and tobacco smoking as well as the presence of existing infection/bacteraemia.<sup>5</sup> Furthermore, operative factors such as groin site surgery, use of

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prostheses, and long surgical procedures contribute to an increased incidence rate of SSI.<sup>5</sup> The consequences of SSI in vascular surgery may be serious, with 30% to 40% of SSI in lower limb bypass procedures resulting in a major amputation.<sup>6</sup> On an individual basis, SSI may cause significant physical or psychological disability.<sup>7</sup> On a population basis, the costs attributed to SSI may be significant, with an estimated cost of £700 million per annum to the National Health Service (NHS) in the UK.<sup>8</sup>

Previous studies have reported estimates of the additional healthcare costs associated with SSI in the NHS. Jenks et al<sup>9</sup> report SSI rates for a range of specialties at a large NHS hospital between April 2010 and March 2012. For vascular surgery, the median excess postoperative length of stay (LOS) associated with SSI was 10 days, and the average cost was £2480 per episode at 2012 prices (£2702 at 2018/19 prices). Coello et al<sup>10</sup> analysed national surveillance data from 140 English hospitals in the period October 1997 to June 2001 for a range of surgical procedures. For vascular surgery, the mean excess LOS associated with SSI was 12.2 days (95% CI 9.8-15.0) and the cost was £3545 per episode at 2003 prices (£3862 at 2018/19 prices). These studies are now quite dated and there is a need to validate results in light of contemporary practice.

A pilot randomised controlled trial (RCT) was conducted to examine the use of post-operative dressings coated with dialkylcarbamoyl chloride (DACC) in the prevention of SSI in primarily closed incisional wounds.<sup>11</sup> The study recruited patients undergoing clean or clean-contaminated vascular surgery. The primary clinical outcome was SSI at 30 days. A 36.9% relative risk reduction was observed in the DACC-coated arm. Overall, the SSI rate across both arms of the trial was 21%. Given the significant morbidity and mortality attached to SSI following vascular surgery as well as the burden on healthcare service providers, it is important to quantify the clinical and economic impact of these infections.

The aim of the current study is twofold. Firstly, to use information from the trial to estimate the cost associated with the development of SSI in relation to length of stay (LOS) and antibiotic treatments. Secondly, to use the same data to assess the relationship between the development of SSI and health-related quality of life (HRQoL). In addition, the study considers the impact of developing SSI on both readmission rates and on patients returning to work.

## 2 | METHODS

Data from 144 patients treated in a tertiary vascular surgery unit in the United Kingdom were collected to determine the impact of DACC-coated dressings on the incidence of SSI.<sup>11</sup> This study was conducted according to

### Key Messages

- Surgical site infections (SSI) in vascular surgery can result in serious consequences on both individual and population basis
- Data from 144 patients treated in a tertiary vascular surgery were used to analyse the effects of SSI. All statistical analyses were performed in R v 3.6.0
- SSI reduce patient health-state utility and have a considerable cost impact for hospital providers through increased length of stay, readmission, and the costs of antibiotics

a previously published protocol.<sup>12</sup> Ethical approval was obtained (16/LO/2135), and the study conduct was in accordance with the Declaration of Helsinki.<sup>13</sup> The study was prospectively registered with <http://clinicaltrials.gov> (NCT02992951). Participants were randomised to postoperative wound dressing with either a DACC-coated occlusive absorbent dressing or a non DACC-coated occlusive absorbent dressing in a 1:1 ratio. Randomisation occurred in the theatre after wound closure to prevent performance bias. The ASEPSIS scoring system was used to assess the wound between postoperative days 5 and 7 and at postoperative day 30 ± 3 days. For further details on data collection methods for the primary outcomes see Totty et al.<sup>11</sup> During the study, data were also collected on a series of secondary outcomes, including antibiotic use, LOS, time taken to return to work, and readmission to hospital. At each study follow-up time point, patient-reported HRQoL was recorded using the EQ-5D-3L instrument.<sup>14</sup>

### 2.1 | Data analysis

Eight of the 144 records were removed prior to data analysis for the following reasons:

- Participant withdrew from the study (n = 4)
- No follow-up data after day 0 (n = 2)
- Incorrect follow-up dates recorded, resulting in returning to work prior to surgery occurring (n = 1)
- SSI reported but no antibiotic treatment information recorded (n = 1)

These records were not excluded from the primary outcomes analysis which focused on the feasibility of conducting a full RCT.<sup>11</sup> A final total of 136 patients were

available for this analysis. Study participants were stratified into those who did not experience SSI within 30 days following surgery (No SSI;  $n = 107$ ) and those who did (SSI;  $n = 29$ ).

Complete EQ-5D records were available at baseline for 73 patients who did not develop SSI and 18 patients who did. At day 30, there were 52 and 9 complete records for patients with no SSI and with SSI, respectively.

Linear models were estimated to control for the impact of multiple independent variables on the average LOS, HRQoL at baseline, and at days 7 and 30. Initial statistical model development found that using a natural logarithmic transformation of the LOS data [ $\ln(\text{LOS} + 1)$ ] resulted in a superior model fit (confirmed by Akaike information criterion (AIC) values and graphically; not presented).

The variables SSI within 30 days, age, sex, body mass index (BMI), smoking status, diabetes, and procedure type were controlled for in the linear model for LOS. Stepwise selection was used to find a subset of variables that resulted in the best-performing model based on AIC. The variables sex, BMI, and diabetes were found to have no significant impact on LOS and therefore removed from the final linear model (stepwise procedure; not presented). The treatment variable, standard or DACC dressing, was controlled for in the linear models for HRQoL but was found to be non-significant and was removed during model refinement from all the linear models for HRQoL. The covariables used in the final statistical models are outlined in Supplementary Table S1. No second-order interactions were considered in the statistical models because of small patient numbers. For all statistical analysis, significance was defined as  $P \leq 0.05$ .

All statistical analyses were performed in R v 3.6.0.<sup>15</sup> Utility values were calculated from the EQ-5D-3L instrument using the UK value set with the R package eq5d v0.7.0.<sup>16</sup>

## 2.2 | Cost analysis

The cost per SSI episode was estimated by adding the inpatient cost (mean additional LOS  $\times$  cost per day) to

the average cost of antibiotics. The cost per inpatient day was calculated from a weighted average of two HRG codes (WHO7C and WHO7D) relating to hospitalisation associated with infection or complications of procedures. Costs were sourced from the 2017/18 NHS Reference Costs<sup>17</sup> and inflated to 2018/19 prices<sup>18</sup> (Table 1). One record had missing data for antibiotic usage and was not included in the cost analysis. This resulted in 28 out of 29 patients in the SSI group who were eligible for weighted cost analysis. Antibiotic costs were calculated as a mean cost per patient for antibiotics prescribed during the study with relevant prices sourced from the BNF.<sup>19</sup>

The effect of LOS on the SSI episode cost was tested in a sensitivity analysis by applying the 95% confidence interval around the unadjusted mean LOS, median LOS, and the mean LOS adjusted for the effects of SSI within 30 days, age, smoking status, and procedure type.

## 3 | RESULTS

Baseline characteristics for the 136 patients included in the analysis are summarised in Table 2. There are no statistically significant differences between groups (SSI vs non-SSI) in age (mean 63.6 vs 62.6 years;  $P = 0.698$ ), sex (males: 79.3% vs 63.6%;  $P = 0.168$ ), or BMI (mean 27.33 vs 28.71;  $P = 0.248$ ). However, there are statistically significant differences in smoking status and diabetes. There are relatively more current smokers in the SSI group ( $P = 0.002$ ) and relatively fewer patients with diabetes ( $P = 0.035$ ). There are also significant differences in the type of surgical procedure ( $P = 0.031$ ) (Table 2).

### 3.1 | Length of stay

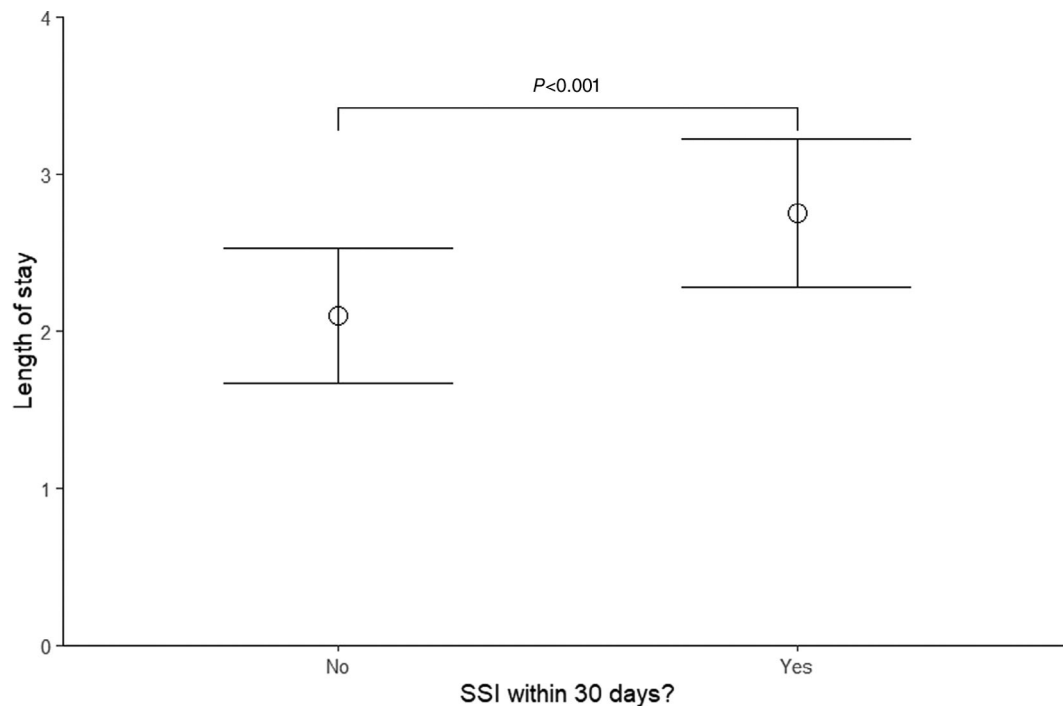
The mean LOS including readmission was 6.52 days (no SSI,  $n = 107$ ) and 16.24 days (SSI,  $n = 29$ ), a difference of 9.72 days (95% CI 5.25-14.18). The median length of stay was 4 days (no SSI) and 11 days (SSI), a difference of 7 days. After controlling for differences in age, smoking status, and procedure type, the presence of SSI

**TABLE 1** Cost of an additional hospitalisation because of infection or other complication per day

Currency Code	Description	Activity	Unit Cost
WH07C	Infection or other complication of procedures, with single intervention, with CC score 2+	1463	£339.23
WHO7D	Infection or other complication of procedures, with single intervention, with CC score 0-1	2888	£330.99
Weighted average	£333.76		

**TABLE 2** Baseline patient characteristics

Characteristic	Patients with no SSI within 30 days (n = 107)	Patients with SSI within 30 days (n = 29)	P Value
Age, years (mean (SD))	62.61 (12.74)	63.62 (11.28)	0.698
Sex, male (%)	63.6	79.3	0.168
BMI (mean (SD))	27.33 (5.44)	28.71 (6.51)	0.248
Smoking status (%)			0.002
Current	15.0	41.4	
Ex	59.8	27.6	
Never	25.2	31.0	
Diabetes (%)			0.035
None	74.7	51.7	
Diet controlled	1.9	6.9	
Tablet controlled	13.1	13.8	
Insulin controlled	10.3	27.6	
Procedure type (%)			0.031
Open surgery on the aorta/ileac vessels	23.4	3.4	
Lower limb arterial surgery	35.5	55.2	
Varicose vein surgery	8.4	10.3	
Major limb amputation	8.4	20.7	
Renal dialysis access	14.0	6.9	
Other	10.3	3.4	



**FIGURE 1** Linear model predicted effect of SSI on the length of stay in hospital. Mean length of stay (LOS) in patients with SSI or no SSI within 30 days of surgery was assessed using a linear model. Model coefficients for the final linear model are presented in Supplementary Table S2. The results show that those with an SSI with 30 days of surgery have a significantly longer LOS compared with those without an SSI ( $P < 0.001$ ). The data are presented as the mean  $\pm$  95% confidence interval from 107 and 29 individual patients. The model prediction was generated considering a patient aged 62.8 years old, who had never smoked and who had open surgery on the aorta/ileac vessels

**TABLE 3** Sensitivity analysis

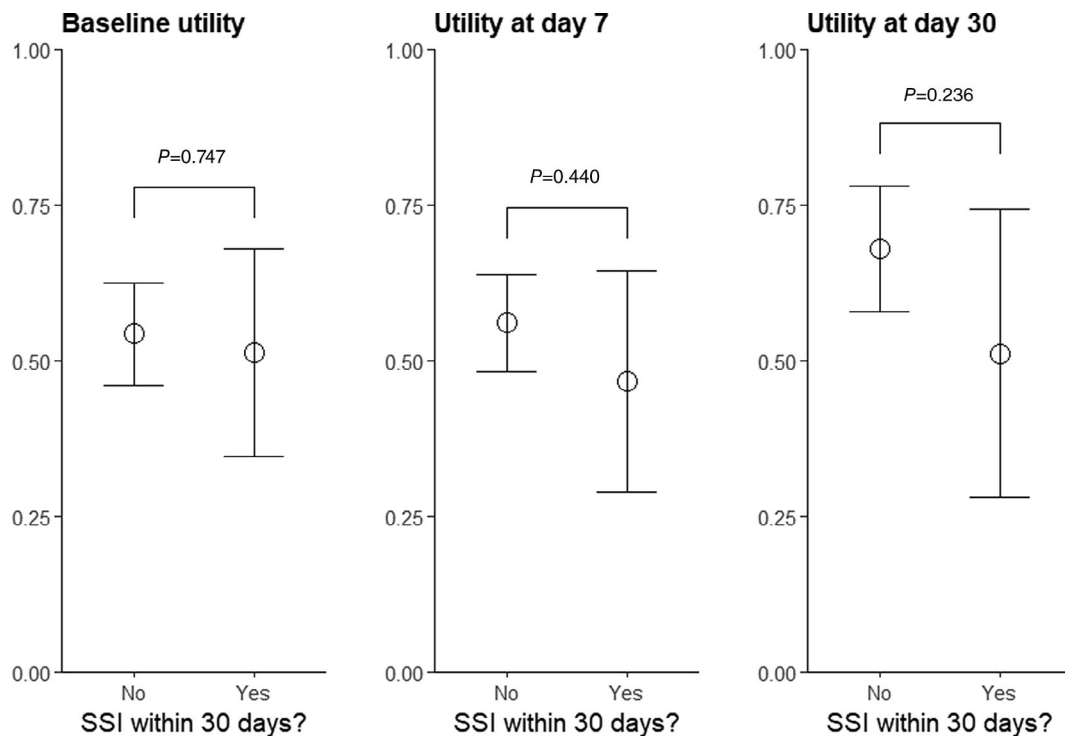
Method	Estimated Difference in LOS	Estimated SSI Episode Cost <sup>a</sup>		
		Mean	Lower 95% CI <sup>b</sup>	Upper 95% CI
Mean	9.72	£3776	£2064	£5488
Median	7.00	£2868	£1533	£3870
Adjusted mean <sup>c</sup>	7.52	£3040	£2038	£4696

Abbreviations: CI: confidence interval; LOS, length of stay; SSI, surgical site infection.

<sup>a</sup>A constant antibiotic cost of £532 was assumed.

<sup>b</sup>Lower and upper interquartile range used for the median estimate.

<sup>c</sup>Based on predictions derived from the linear model with procedure type set to “open surgery on the aorta/ileac vessels”.



**FIGURE 2** Linear model predicted effect of SSI on utility at baseline, day 7 and day 30. Mean utility in patients with SSI or no SSI within 30 days of surgery was assessed using a linear model at days 0, 7 and 30. Model coefficients for the final linear models are presented in Supplementary Table S4. The results show a non-significant trend of reduction in utility score over time in those with SSI compared with those without SSI. The data are presented as the mean  $\pm$  95% confidence interval from 73 and 18 individual patients at baseline, 59 and 8 individual patients at day 7 and 52 and 9 individual patients at day 30. The model predictions were generated using the mean baseline utility for day 7 and day 30 predictions

at 30 days was associated with a statistically significant 92% increase in LOS (7.52 days;  $P < 0.001$ ; result on the untransformed scale; Figure 1). Model coefficients are displayed in Supplementary Table S2.

### 3.2 | SSI episode cost

The weighted cost of hospitalisation because of infection or other complication in the NHS is £333.76 per day (Table 1). Assuming the SSI-associated LOS is the difference in mean LOS between the two groups, the estimated inpatient cost

for an episode of SSI is £3244 (£333.76 \* 9.72 days). The mean cost of antibiotic treatment for SSI was £532. Adding this to the inpatient cost gives an estimate of the total cost of £3776 per episode. However, it should be noted that the costs of antibiotics are heavily skewed. The median antibiotic cost per patient is £10.72 (IQR: £2.69-£119.73) but five patients account for 94% of the total antibiotic costs, and two patients had antibiotic costs in excess of £4000 each (see Supplementary Table S3 for all patient antibiotic costs). The SSI-associated LOS adjusted for age, smoking status and procedure type was 7.52 days, and the adjusted episode cost including antibiotics was £3040.

**TABLE 4** Number of patients readmitted to hospital or returned to work

Readmitted to hospital within 30 days		
	No readmission	Readmission
No infection (n = 107)	101	6
Infection (n = 29)	23	6
Returned to work within 90 days		
	Did not return to work	Returned to work
No infection (n = 60)	34	26
Infection (n = 24)	22	2

As a sensitivity analysis the mean additional LOS (9.72 days), the median additional LOS (7.00 days) and the mean adjusted additional LOS (7.52 days) were varied within their respective 95% confidence intervals. The mean cost of antibiotics was not changed. Episode cost estimates range from £1533 to £5488 (Table 3).

### 3.3 | Health-related quality of life

Baseline utility scores for patients in the two groups were similar (0.54 and 0.51 in the no SSI and SSI group respectively;  $P = 0.747$ ). Mean utility scores at day 7 and day 30 were 0.56 (no SSI) vs 0.47 (SSI), and 0.68 (no SSI) vs 0.51 (SSI), respectively (Figure 2). There is a trend increase in utility for patients not developing SSI and a non-significant trend decrease for patients with SSI between baseline and day 30 ( $P = 0.236$ ). Differences between the two groups are not statistically significant at any timepoint. Model coefficients are displayed in Supplementary Table S4.

### 3.4 | Readmissions

The number of patients readmitted to hospital within 30 days of the index procedure and the number of patients who returned to work within 90 days are shown in Table 4. Patients with SSI had relative odds of 4.39 (95% CI; 1.30-14.86) to be readmitted to hospital compared with patients without SSI (21% readmitted vs 6%, respectively).

### 3.5 | Return to work

Patients with SSI had relative odds of 0.12 (95% CI; 0.03-0.55) for return to work within 90 days of the index

procedure compared to those who did not have SSI (8% returned to work vs 43%, respectively) (Table 4). The mean number of days until return to work, conditional on returning to work, for a patient without SSI was 16.58 (95% CI 12.54-20.62) compared with 25.5 (95% CI 16.68-34.32) for a patient with SSI. Because only two patients in the infection group returned to work within the study period, it was not possible to perform any statistical analysis to compare the two groups.

## 4 | DISCUSSION

This study provides insight into the clinical and economic burden associated with SSI in one large NHS teaching hospital. In a sample of 136 patients undergoing vascular surgery, 21% developed SSI which was associated with a mean increase in LOS of 9.72 days and an average cost of £3776 per episode. These results are consistent with previous studies<sup>9,10</sup> but we note that previous studies did not control for potential confounding variables, and for this reason the present study may provide a more robust estimate of the impact of SSI on length of stay. In this study population, age and the type of vascular procedure were found to be significantly associated with length of stay, but conversely smoking status, BMI, and the presence of diabetes were not. After adjusting for potential confounding factors SSI is still associated with a more than 90% increase in length of stay (on the untransformed scale).

This study has also highlighted the importance of antibiotic costs which are often overlooked. The main driver of cost for most patients is prolonged LOS. However, for a minority of patients, antibiotic costs are the most significant component. In the present sample, 18% of patients (five patients) accounted for more than 90% of antibiotic costs, and two patients had costs in excess of £4000. High-cost patients are likely to be those with a resistant infection, or those with a deep infection involving a prosthetic graft, who may have been unsuitable for explanation, which in itself would be a costly surgical procedure. Previous studies have demonstrated that antibiotic-resistant SSIs, and antibiotic resistance generally, can add considerable treatment costs.<sup>20-22</sup>

The odds of readmission in the SSI group were higher, and the development of SSI was shown to potentially lead to a reduction in the rate of return to work. Of the patients who did not develop SSI, 6% were readmitted and 44% returned to work within 90 days compared with 21% readmitted and 8% returned to work for patients with SSI. In principle delayed return to work would impose social costs in terms of lost productivity.<sup>23,24</sup> However, in the present sample because of the average

age of the patients (63 or 64 years) many would not be expected to be working in any case.

The analysis here relates solely to costs incurred in the hospital for infections diagnosed before discharge, or for infections requiring readmission. Many surgical infections are diagnosed after discharge and managed in the community, and for this reason the estimates here do not represent the overall impact of SSI on the NHS. It is estimated that approximately 11% of the costs of SSI fall on the community or on the patient.<sup>25</sup> Future studies might capture the true cost impact by linking primary care records in the Clinical Practice Research Datalink (CPRD) database with Hospital Episode Statistics (HES) in order to trace the impact on both secondary and primary care services.

The presence of SSI was associated with a reduction of 0.156 at day 30 ( $P = 0.236$ ) in patient-reported health-state utility measured by EQ-5D-3L compared to the no SSI group. Utility declined over time for patients with SSI in contrast to other patients whose utility increased but these trends were not statistically significant. The study was not powered to detect differences in HRQoL and the number of complete records was limited. A previous systematic review of the literature concluded that SSI has a clinically significant impact on health-state utility and HRQoL.<sup>26</sup> Three patient-level studies<sup>27-29</sup> reported EQ-5D utility values associated with SSI, with a utility decrement ranging from 0.102 to 0.124.

This study adds to the current evidence base showing a substantial impact of SSI on patients and on healthcare systems and provides fresh insight into the impact of SSI within vascular surgery. The overall SSI rate in this study is in line with SSI incidence quoted in the literature.<sup>2-4</sup> While there is a significant financial cost associated with an increase in LOS, this also puts patients at an increased risk of further complications, such as longer overall recovery times and further non-SSI infections including respiratory and urinary tract infections.<sup>30</sup> Other consequences of prolonged hospital stay include pressure-related skin damage, venous thromboembolism, deconditioning and an increase in frailty, and ultimately an increase in mortality. At an institutional level, delayed discharge and higher readmissions limit the availability of beds and theatre resources, lengthen waiting lists and delay admissions from the emergency department, potentially severely impacting care.

On an individual basis, SSI may have devastating consequences, impacting on both the physical and mental health of patients during their inpatient stay and following discharge.<sup>7</sup> Physical disability and symptoms of depression have been shown to be related, and up to half of patients with depression during hospitalisation have been shown to remain depressed at 6 months post-

discharge.<sup>31</sup> The effect of SSI on mental and physical health may produce further, unmeasured financial costs to both the patient and healthcare services in terms of additional treatments required for indirect and direct consequences of developing infection.

In conclusion, the results of this analysis and other studies indicate that SSI has a considerable cost impact for hospital providers through increased length of stay, readmission and the costs of antibiotics. Existing strategies to reduce the risk of SSI are not benefitting high-risk vascular patients and future interventions should therefore be investigated in detail. These interventions should be explored with robust, well-conducted clinical trials.

## CONFLICT OF INTEREST

One author acted as a consultant to Essity. All other authors declare no conflict of interests.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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